Tom,
Yours.

Department of Energy
Germantown, MD 20874-1290

FEB 2 5 1997

Dr. Richard Setlow
Brookhaven National Laboratory
P.O. Box 5000, Building 460
Upton, New York 11973-5000

Dear Dr. Setlow:

During the recent Republic of the Marshall Islands (RMI) and Department of Energy (DOE) meeting in Majuro held January 28-30, 1997, the Rongelap Local Government Council requested the identity of Rongelap individuals who were administered radioactive tritium and chromium-51 and information on the associated administrative techniques or use as described on page 30 of the DOE report entitled, "Human Radiation Experiments Associated with the U.S. Department of Energy and Its Predecessors", published in July 1995.

To provide you with information on this request, I enclose five separate enclosures. The first consists of pages 39 and 40 from the Brookhaven National Laboratory (BNL) report entitled, "Medical Survey of the People of Rongelap and Utirik Islands Nine and Ten Years After Exposure To Fallout Radiation (March 1963 and March 1964), BNL publication number 908(T-371). A table that appears on page 39 of this report identifies by patient number, those Marshallese administered tritium and chromium-51. Similarly, the second enclosure consists of pages 57, 58 and 149 from the BNL report entitled, "Medical Survey of the People of Rongelap and Utirik Islands Eleven and Twelve Years After Exposure to Fallout Radiation (March 1965 and March 1966), BNL publication number 50029(T-446). A table that appears on page 149 of this report also identifies by patient number those Marshallese administered tritium and chromium-51. In addition, the third enclosure consists of pages 31 and 32 from the BNL report entitled, "Medical Survey of Rongelap People Eight Years After Exposure to Fallout", BNL publication number 780 (T-296). A table appears on page 31 of this report which indicates by initial the Micronesians or Caucasians that were living in the Marshall Islands at the time and participated in the Cr-51 blood volume determinations.

The fourth enclosure is a copy of a technical data sheet on the use of chromium-51 for diagnostic procedures. The fifth enclosure is a copy of a Cr-51 proposal (dated July 29, 1955) submitted to and approved by the BNL Committee on Use of Radioactive Isotopes in Humans. This proposal is provided as an initial reference to help determine the medical status (i.e., experimental or clinical diagnostic procedure) on the use of Cr-51 in the early 1960's. Note also that the proposal references a 1953 medical journal citation.

I request that BNL provide the following information:

1. The names of the Marshallese who were identified by BNL patient number or initials in the three tables;

2. Documentation to demonstrate whether the chromium-51 and tritiated water techniques were "experimental" or medically accepted diagnostic procedures at the time of their use from 1961 to 1963.

Please forward this information to me by March 15, 1997. I will then forward to the Rongelap Atoll Local Government Council along with other documents pertinent to their request.

Sincerely,

R. T. Bell

R. Thomas Bell, III
Supervisor
Pacific Health Programs
Office of International
Health Programs

Enclosures

cc w/enclosures:
The Honorable Banny de Brum,
Republic of the Marshall Islands
Senator Johnsay Riklon,
United States Senate
Mayor James Matayoshi,
Rongelap Atoll Local Government Council
Mr. Gordon Benjamin,
Rongelap Atoll Local Government Council

Enclosure 1

BNL 900 (T-371)

MEDICAL SURVEY OF THE PEOPLE OF RONGELAP AND UTIRIK ISLANDS NINE AND TEN YEARS AFTER EXPOSURE TO FALLOUT RADIATION (MARCH 1963 AND MARCH 1964)

ROBERT A. CONARD, M.D., LEO M. MEYER, M.D., WATARU W. SUTOW, M.D., AUSTIN LOWREY, M.D., BRADFORD CANNON, M.D., WILLIAM C. MOLONEY, M.D., ALVIN C. WATNE, M.D., ROBERT E. CARTER, M.D., AROBATI HICKING, PRACTITIONER, RICHARD HAMMERSTROM, PH.D., BYRON BENDER, PH.D., ISAAC LANWI, PRACTITIONER, EZRA RIKLON, PRACTITIONER, AND JETON ANJAIN, PRACTITIONER

BROOKHAVEN NATIONAL LABORATORY

ASSOCIATED UNIVERSITIES, INC.

under contract with the

UNITED STATES ATOMIC ENERGY COMMISSION

Bone Marrow Examinations

The differential counts of bone marrow aspirations on 6 individuals, 4 exposed and 2 unexposed, are listed in Appendix 18. The differential counts showed that in 3 of 4 exposed persons there was an alteration in the myeloid-erythroid ratio manifested by an increased number of red cell precursors. In addition to hyperplasia, abnormalities of chromatin material with double nuclei and increased numbers of mitotic figures were seen in the normoblastic series (Figures 50 and 51). One of the exposed (No. 63) and one of the unexposed (No. 948) showed increased lymphocytosis of 33% and 27% respectively. This was reflected in the peripheral blood counts in which the total number of leukocytes was normal but the lymphocytes were increased to 51% and 56%. The significance of this finding remains obscure, but repeat bone marrow examinations will be carried out in both these cases during the 1965 survey.

Red Cell Mass and Plasma Volume Studies

During the 1961 and 1962 surveys blood volume studies were performed on a group of Marshallese subjects and on a small number of Caucasians who had been living on the islands for one year or longer. Sodium chromate labeled with Cr^{51} was used to tag the erythrocytes. With body weight as a criterion, it appeared that 15 of 23 subjects, both Marshallese and Caucasian, showed a significant reduction in red cell mass and/or plasma volume.

In order to establish the relationship of blood volume to lean body mass tritiated water was administered orally to each of 21 Marshallese subjects during the 1963 survey. In addition, determinations were made of red cell mass and blood volume by using Cr^{51}-labeled sodium chromate.

Table 20

Total Blood and Red Cell Volume Data
(WT. = gross weight; TBW = total body water; FAT = fat as % gross weight; LBM = lean body mass; RCV = red cell volume; BV = blood volume)

Subject No.	WT., kg	TBW, l	TBW, %	FAT, %	LBM, kg	RCV, l	BV, l	RCV/LBM, ml/kg	BV/LBM, ml/kg
822	54.54	38.1	68.8	4.4	52.1	1.402	3.260	26.9	62.6
832	46.36	25.0	53.0	26.4	34.1	0.849	2.358	24.9	69.2
836	56.36	35.3	61.7	14.3	48.3	1.428	3.320	29.6	68.7
838	66.13	41.7	62.2	13.6	57.1	2.108	4.053	36.9	71.0
841	66.81	31.9	47.0	34.7	43.6	1.150	3.196	26.4	73.3
873	61.36	43.2	69.4	3.6	59.1	1.670	3.631	28.3	61.4
881	68.63	32.8	47.1	34.6	44.7	1.996	4.247	44.7	95.0
882	54.77	39.9	71.8	0.3	54.6	1.131	3.426	20.7	62.7
885	61.81	41.0	65.3	9.3	56.1	1 760	3.825	31.4	68.2
895	55.90	29.0	51.5	28.5	40 0	1.070	2.488	26.8	62.2
916	63.63	32.6	50.4	30.0	44.5	1.091	3.031	24.5	68.1
928	57.27	29.4	50.5	29.9	40.2	0.927	2.505	23.1	62.3
932	46.30	26.2	55.7	22.6	35.8	1.274	2.963	35.6	82.8
938	40.00	22.0	54.1	24.9	30.1	0.886	2.331	29.4	77.4
942	57.72	27.6	47.1	34.6	37.8	0.860	2.150	22.8	56.9
959	60.00	32.2	52.8	26.7	44.0	1.151	2.877	26.2	65.4
960	38.63	24.8	63.1	12.4	33.9	0.774	2.150	22.8	63.4
1007	71.36	41.2	56.9	21.0	56.4	1.620	4.155	28.7	73.7
1043	41.81	26.4	62.3	13.5	36.2	1.066	2.664	29.4	73.6
1501	66.81	43.3	64.0	11.2	59.3	1.843	3.840	31.1	64.8
Jeton	63.18	39.8	61.9	14.0	54.4	1.310	2.675	24.1	49.2
Av		33.5				1.303	3.102	28.3	68.2

$\frac{\text{Av RCV (l)}}{\text{Av TBW (l)}} = 0.039$; $\frac{\text{Av BV (l)}}{\text{Av TBW (l)}} = 0.092$

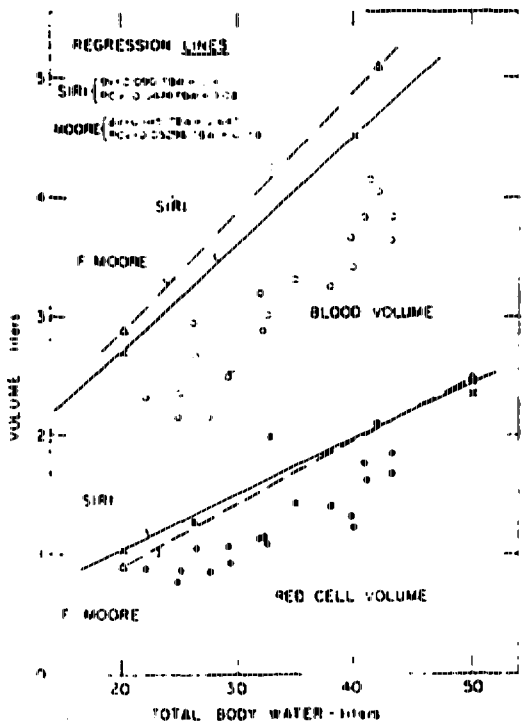


Figure 52.

After 4 hours, urine samples were collected and lyophilized, and tritium in the water portion was counted in a Nuclear-Chicago liquid scintillation counter. From these values of total body water, fat was estimated by the formula % fat = 100 − (% TBW/0.72). The % TBW is total body water (in kg) as percent of gross weight. Lean body mass (LBM) was taken as the difference between gross weight and fat (kg).

The data are shown in Table 20. According to Siri (personal communication) the values for total body water, fat, or lean body mass are not different from averages for Caucasian subjects in the San Francisco area. Figure 52 shows the values of blood volume (liters) and red cell volume (liters) plotted against total body water. Regression lines drawn for Caucasians by Moore[43] and Siri (unpublished) disclose that with the exception of one case the values of Marshallese fall far below those described by the authors. The average red cell volume for Marshallese is 28.3 ml per kg LBM as compared to 35 ml/kg (Siri, unpublished).

Whether these findings represent a genetic difference or are the result of environment and/or diet cannot be stated at present. It is hoped that studies will be continued in 1965 with examinations of blood volume and total body water in Caucasians living in this area for one year or more.

Table 21

Protein Bound Iodine, 1963 and 1964

Subject No.	PBI, γ %
Marshallese Residing on Rongelap	
1	9.4
6	7.9
10	12.0
14	8.2
86	8.2
17	6.8
21	8.1
69	10.2
865	8.2
Av	8.8
Marshallese Residing on Ebeye	
12	8.8
829	7.1
944	2.0
938	5.6
982	6.3
950	6.7
1005	7.9
1043	5.8
Av	6.3
Americans Residing in Marshall Islands at Least 1 Year	
	6.2
	5.5
	5.0
	5.6
	6.1
	5.5
	4.4
Av	5.5
Medical Team	
	4.7
	4.7
	5.1
	5.5
	5.2
	2.5
	6.0
	4.5
	4.2
	6.9
Av	4.9

Other Laboratory Studies

Chromosome Studies. Microscopic examination of smears from peripheral blood cultures is in

Enclosure 2

BNL 50029 (T-446)

The Medical Research Center

Brookhaven National Laboratory

Upton, L. I., New York

MEDICAL SURVEY OF THE PEOPLE OF RONGELAP AND UTIRIK ISLANDS ELEVEN AND TWELVE YEARS AFTER EXPOSURE TO FALLOUT RADIATION (MARCH 1965 AND MARCH 1966)

ROBERT A. CONARD, M.D., LEO M. MEYER, M.D., WATARU W. SUTOW, M.D., JAMES S. ROBERTSON, M.D., PH.D., JOSEPH E. RALL, M.D., PH.D., JACOB ROBBINS, M.D., JOHN E. JESSEPH, M.D., JOSEPH B. DEISHER, M.D., AROBATI HICKING, PRACTITIONER, ISAAC LANWI, PRACTITIONER, ERNEST A. GUSMANO, PH.D., AND MAYNARD EICHER

BROOKHAVEN NATIONAL LABORATORY

ASSOCIATED UNIVERSITIES, INC.

under contract with the

UNITED STATES ATOMIC ENERGY COMMISSION

Rongelap as a result of their fallout radiation exposure. Attempts at 8 and 9 years post exposure to obtain suitable blood cultures had not been entirely successful. However, during the 10-year survey a slight modification of the Moorehead technique[15] resulted in a series of satisfactory cultures on 51 people: 30 in the higher exposure group (175 rads), 13 in the lower exposure group (69 rads) and 8 from the unexposed Rongelapese who were on another island at the time of the accident. The detailed results of these studies are presented in Appendix 14.*

Table 25 summarizes the results. A higher incidence of aneuploid cells was noted in the exposed group, but the difference was not great enough to be significant. Unexpectedly, the lower exposure group showed more aberrations than did the more heavily exposed group, and the latter group showed even less aberrations than the unexposed. However, the incidence of 2-hit aberrations was significantly higher ($p < 0.004$) in the exposed groups and did appear to be radiation induced. Figure 66 shows a dicentric and a ring form noted in chromosome spreads from two exposed individuals.

OTHER LABORATORY STUDIES

Total Blood Volume and Red Cell Volume

Previous studies (1961, 1962) with ^{51}Cr-labeled erythrocytes on Marshallese subjects living in their native environment have shown reduced red cell mass and/or total blood volume with total body weight used as a base line. During the 1963 survey, similar studies were performed on 21 Marshall Islanders, but these data were related to total body water as determined by tritiated water.[10] Results showed that in all instances but one the values for red cell mass and total blood volume fell below normal levels for persons living in temperate zones of the United States.

The present study was undertaken during the surveys in 1965 and 1966. A total of 19 Caucasian Americans (3 females and 16 males) living in the Marshall Islands for periods of 3 months to 9 years were examined by the same techniques.* The results of these studies on each individual are presented in Appendix 15, along with data on the 21 Marshallese in whom these studies were carried out in 1963. The data were programmed and analyzed by a high speed digital computer. Regression lines obtained for the Caucasians and the Marshallese are presented in Figure 67 along with regression lines of Moore[16] and Siri[17] for Americans.

The Marshallese regression lines for both blood volume and red cell colume have very nearly the same slopes as the lines of the Siri and Moore groups, but they are significantly below the latter (significant at the 1% level). The Caucasians living in the Marshall Islands also show regression lines for blood volume and red blood cell volume with slopes similar to those of the Marshallese and the Siri and Moore groups. Comparison of the regression lines shows no significant difference between

*We are grateful to Dr. Shields Warren and his group at the Cancer Research Institute in Boston for carrying out the chromosome analyses.

*We are grateful to Dr. W. E. Siri, University of California, for carrying out the tritium-water analyses.

Table 25

Summary of Chromosome Findings

Group	No. of persons	No. of cells scored	Percent of cells with 2n=46	No. of persons with aberrations	Chromosome aberrations				Total aberrations	Total cells with aberrations	Chromatid breaks	Isochromatid gaps
					Fragments	Dicentrics	Rings	Exchanges				
Exposed 175 rads	30	1500	10	12 (40%)	11	6	-	5	22 (1.46%)	20 (1.33%)	43	15
Exposed 69 rads	13	650	5	11 (84.6%)	10	2	1	8	21 (3.23%)	18 (2.77%)	31	4
Unexposed	8	400	5.5	5 (62.5%)	9	-	-	-	9 (2.25%)	8 (2.0%)	6	3

the blood volumes and the red cell volumes of the Caucasians living in the Islands and the Caucasians of the Siri and Moore groups; furthermore, duration of residency in the Islands has no significant effect. Earlier data had suggested that Caucasians living in the Marshall Islands might have reduced blood volumes and red blood cell volumes. Though this may be true for certain individuals, it does not seem to hold true for the group as a whole.

Test for Australia Antigen

The Australia antigen, a serum protein first detected in the serum of the Australian aborigines, was searched for in the Rongelap population.* Details of these studies are presented in Appendix 16. Samples of sera from 250 Rongelap people were examined between 1958 and 1965. Of these, 237 were consistently negative, 11 were consistently positive (4.4%), and 2 were inconsistent. Family studies indicated that positive subjects were homozygous for the genes. This antigen has been found to be relatively common in some forms of leukemia. Since the Rongelap people will be medically examined for many years, it will be interesting to see whether the presence of this antigen is related substantially to disease, particularly leukemia.

*These studies were carried out by Dr. B.S. Blumberg, Institute for Cancer Research, Philadelphia, Pa.

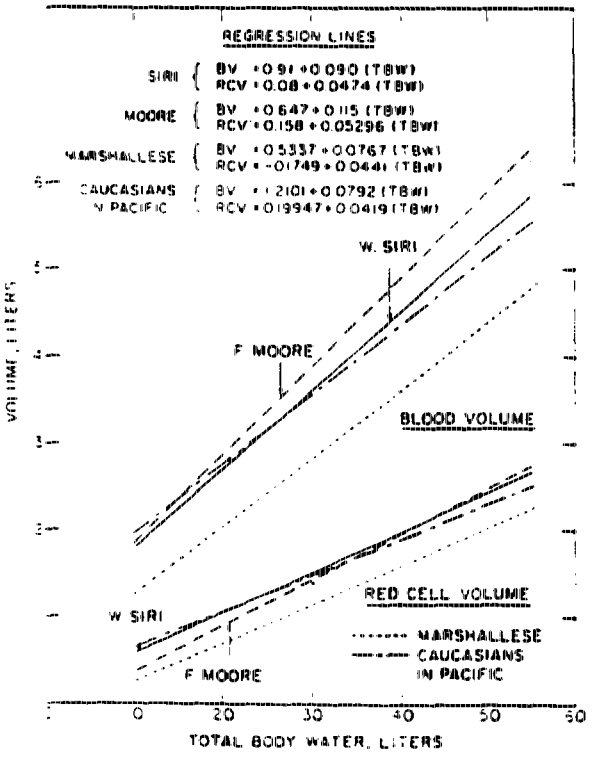


Figure 67.

ESTIMATION OF INTERNAL BODY BURDENS OF RADIONUCLIDES

In the 1965 survey, the body burdens of radionuclides were determined by use of a portable shadow-shield type of whole-body counter and by radiochemical analysis of 24-hr urine specimens.

Whole-Body Counting

The use of the shadow-shield type of whole-body counter represents a departure from previous surveys, in which a 21-ton steel room had been transported to Rongelap and used for this purpose. Correlations between the two techniques were established by standardizations using the permanent steel room and a duplicate of the shadow shield at Brookhaven National Laboratory. The body ^{40}K values of the Rongelapese provide another means of correlation.

The shadow-shield counter (Figure 68) is very similar to the one described by Palmer and Roesch[18] and to the Hanford whole-body counter.[19] It was installed on Rongelap in one of the newly acquired air-conditioned trailers. The detector, an 11½-in.-diameter NaI (Tl) crystal 4 in. thick (Harshaw), is housed in a lead shielding supported by a steel plate about 14 in. above the bed. The subject to be counted lies on a foam rubber cushion in the trough between the two walls of lead bricks, and is moved to a position under the detector by a motor-driven worm-screw drive. The system was calibrated with a plastic phantom man, both in a stationary position beneath the counter and with movement equivalent to the length of the body during the count.

The signal from the detector was picked up by 7 photomultiplier tubes mounted on the crystal, and the gamma-ray spectrum was analyzed with a 400-channel pulse-height analyzer (RIDL). The gamma-ray spectral data were read out on rolls of adding-machine paper for immediate evaluation, and on punched paper tape for subsequent data processing which involved transfer of the data from the punched paper tape to magnetic tape and subsequent analysis in terms of radioisotopes by a spectral stripping program on an IBM-7094

APPENDIX 15

Total Blood and Red Cell Volume Data

(WT=gross weight; TBW=total body water; FAT=fat as % gross weight; LBM=lean body mass; RCV=red cell volume; BV=blood volume)

Subject No.	WT (kg)	TBW (l)	TBW (%)	FAT (%)	LBM (kg)	RCV (l)	BV (l)	RCV/LBM (ml/kg)	BV/LBM (ml/kg)
				A - Marshallese					
822	54.54	38.1	68.8	4.4	52.1	1.402	3.260	26.9	62.6
832	46.36	25.0	53.0	26.4	34.1	0.849	2.358	24.9	69.2
836	56.36	35.3	61.7	14.3	48.3	1.428	3.320	29.6	68.7
838	66.13	41.7	62.2	13.6	57.1	2.108	4.053	36.9	71.0
841	66.81	31.9	47.0	34.7	43.6	1.150	3.196	26.4	73.3
873	61.36	43.2	69.4	3.6	59.1	1.670	3.631	28.3	61.4
881	68.63	32.8	47.1	34.6	44.7	1.996	4.247	44.7	95.0
882	54.77	39.9	71.8	0.3	54.6	1.131	3.426	20.7	62.7
885	61.81	41.0	65.3	9.3	56.1	1.760	3.825	31.4	68.2
895	55.90	29.0	51.5	28.5	40.0	1.070	2.488	26.8	62.2
916	63.63	32.6	50.4	30.0	44.5	1.091	3.031	24.5	68.1
928	46.30	26.2	55.7	22.6	35.8	1.274	2.963	35.6	82.8
938	40.00	22.0	54.1	24.9	30.1	0.886	2.331	29.4	77.4
942	57.72	27.6	47.1	34.5	37.8	0.860	2.150	22.8	56.9
959	60.00	32.2	52.8	26.7	44.0	1.151	2.877	26.2	65.4
960	38.63	24.8	63.1	12.4	33.9	0.774	2.150	22.8	63.4
1007	71.36	41.2	56.9	21.0	56.4	1.620	4.155	28.7	73.7
1043	41.81	26.4	62.3	13.5	36.2	1.066	2.664	29.4	73.6
1501	66.81	43.3	64.0	11.2	59.3	1.843	3.840	31.1	64.8
2000	63.18	39.8	61.9	14.0	54.4	1.310	2.675	24.1	49.2
	MEAN	33.5				1.303	3.102	28.3	68.2
				B - Caucasians Residing in Pacific Ocean Area					
G.B.	104.55	52.7	49.65	31.0	72.1	2.425	5.390	33.6	74.8
D.B.	71.36	45.9	63.34	12.0	62.8	1.747	3.970	27.8	63.2
J.C.	75.91	45.2	58.56	18.6	61.7	1.809	4.308	29.3	69.8
P.C.	68.18	36.0	52.10	27.6	49.3	1.588	3.379	32.2	68.5
A.C.	90.91	55.2	59.88	16.8	75.61	2.097	5.116	27.7	67.7
W.D.	84.09	51.9	60.73	15.6	70.9	2.412	5.610	34.0	79.1
R.J.	86.36	50.2	57.18	20.5	68.6	2.457	5.341	35.8	77.9
D.J.	70.45	44.3	61.83	14.1	60.5	1.794	4.078	29.7	67.4
C.P.	84.09	43.8	51.23	28.8	59.8	2.657	5.776	44.4	96.6
J.S.	84.09	50.8	59.47	17.4	69.5	2.428	5.518	34.9	79.4
C.T.	80.91	44.6	54.25	24.6	61.0	2.540	5.405	41.6	88.6
A.T.	61.36	37.5	60.19	16.4	51.3	1.199	4.064	23.3	79.2
I.W.	77.27	50.1	63.74	11.4	68.4	2.575	5.479	37.6	80.1
A.B.	65.91	33.9	50.69	29.6	46.4	1.986	4.225	42.8	91.1
T.B.	67.27	33.8	49.44	31.3	46.2	1.424	3.561	30.8	77.1
B.C.	60.00	30.7	50.40	30.0	42.0	1.714	4.181	40.8	99.5
C.M.	60.91	32.1	51.98	27.8	44.0	1.672	4.181	38.5	95.0
D.P.	52.27	27.8	52.42	27.2	38.1	1.149	3.023	30.2	79.3
P.R.	72.73	42.8	57.98	19.5	58.5	2.006	4.458	34.3	76.2
	MEAN	42.6				1.983	4.582	34.2	79.5

ENCLOSURE 3

MEDICAL SURVEY OF RONGELAP PEOPLE EIGHT YEARS AFTER EXPOSURE TO FALLOUT

ROBERT A. CONARD, M.D., LEO M. MEYER, M.D.,
WATARU W. SUTOW, M.D., WILLIAM C. MOLONEY, M.D.,
AUSTIN LOWREY, COL. (MC) USA, A. HICKING, PRACTITIONER,
AND EZRA RIKLON, PRACTITIONER

January 1963

BROOKHAVEN NATIONAL LABORATORY
ASSOCIATED UNIVERSITIES, INC.
under contract with the
UNITED STATES ATOMIC ENERGY COMMISSION

Table 14

Abnormal Chromosomes in Peripheral Blood Cultures

Subject No.	Total counts	Dicentrics	Other
64	2	—	—
10	59	—	—
11	24	—	—
14	26	1	—
27*	30	1	1 minute
41	27	—	—
50	69	—	—
58	32	—	—
69	19	—	—
79	19	—	—
80	16	—	—

*Bone marrow smears showed 3 dicentrics on scanning.

small amounts, however, and glycosuria was demonstrated only in those that showed urine elevations of 2+ to 4+. Four urines showed a slight amount of protein, but other examinations did not reveal abnormalities which might be associated with proteinuria.

Blood Sugar Determinations

Fasting blood sugar analyses were carried out on 8 people (all in the unexposed group) who had shown urine positive for sugar on the previous survey. Of these, 4 showed elevated levels (Nos. 853, 884, 893, and 991). Non-fasting blood sugar determinations were carried out routinely on 72 people in the exposed and 125 in the unexposed groups. Elevations >160 mg % were found in 4 of these, 1 exposed (No. 29) and 3 unexposed (Nos. 932, 936, and 1042). The somewhat higher incidence of diabetes in the Marshallese people has been commented on in previous reports.

Protein-Bound Iodine

Since previous survey results had shown protein-bound iodine levels on the high side of normal, 14 sera were obtained on individuals for repeat analyses this year. The levels varied between 4.6 and 12.0 μg % with a mean of 8.6; these are again generally on the high side of normal.

Table 15

Blood Volume Studies (1961, 1962)

Subject	Race*	Wt., lb	Increase, cc RBC	Increase, cc Plasma	Decrease, cc RBC	Decrease, cc Plasma
P.C.	C	158	—	—	100	750
H.M.	C	105	—	250	100	—
A.	C	153	—	—	400	600
B.W.	C	161	—	—	550	1000
S.S.	C	165	—	—	350	600
H.	C	156	—	—	250	100
L.C.	C	110	—	—	250	500
Em.	M	172	—	—	250	500
B.	M	150	—	—	—	100
S.	M	138	100	—	—	—
Ed.	M	155	—	—	250	100
T.	M	122	—	—	550	600
A.	M	102	—	—	400	—
Sh.	M	109	—	—	300	200
Af.	M	126	—	—	300	—
J.	M	135	—	—	200	150
El.	M	140	—	—	600	500
Me.	M	123	123	100	—	—
K.	M	140	—	—	200	700
Ja.	M	132	—	—	800	770
R.	C	156	—	—	450	400
F.	C	183	—	—	400	700
Mac.	C	—	—	—	200	200

*C = Caucasian, M = Micronesian.

Total Urine Iodine and Creatinine

The purpose of these analyses was to determine whether the rather high protein-bound iodine levels reported in the Marshallese might be related to high iodine levels in the diet. Total iodine and creatinine analyses were carried out on 10 urine samples obtained from subjects who had previously shown relatively high protein-bound iodine levels. The levels for total iodine varied between 5.2 and 66.0 μg % (av. 18.6), and the creatinine levels varied between 0.025 and 0.80 g/l (av. 0.52). These levels were considered to be in the normal range, although the creatinine levels were somewhat high because of alkalinity of the urine samples. Therefore it did not appear that the iodine in the diet could account for the generally higher protein-bound iodine levels observed. The cause of this slight elevation remains to be clarified.

Table 16

Immunoelectrophoretic Analyses

Findings	Subject Nos.
Normal	15, 30, 20, 78, 8, 76, 92, 77, 9, 14, 33, 16, 2, 21, 57, 47, 4, 37, 10, 73, 12, 914, 835, 838, 875, 844, 865, 896, 982, 836, 832, 936, 955, 956, 957, 830, 960, 939, 893, 979, 840, 833, 915, 967, 975, 882, 898, 1005, 868, 822, 1042, 841, 825, 885
Slightly increased γ globulin precipitation-line	53, 71, 86, 52, 63, 22, 32, 87, 59, 54, 79, 6, 66, 1, 45, 928, 856, 883, 940, 1036, 944, 992, 858, 813, 864, 853, 887, 942, 829, 820, 828, 924, 961, 969, 895, 855, 884
Markedly increased γ globulin precipitation-line	862, 891
Slightly increased precipitation-lines for β_{2A}, β_{2M}, and γ	34, 75, 27, 817, 998, 888, 814
Markedly increased precipitation-lines for β_{2A}, β_{2M}, and γ	64, 958, 1035
Markedly increased precipitation-lines for β_{2M} and γ	829, 892, 1001
Slightly increased precipitation-lines for β_{2A} and γ	3, 41
Markedly increased precipitation-lines for β_{2A} and γ	897
Slightly decreased precipitation-line for β_{2M}	5, 900
Slightly increased precipitation-line for β_{2M}	29, 852
Decrease of β_{2A} and slight increase of γ globulin precipitation-lines	866
Decrease of β_{2A} and γ globulin precipitation-lines	60, 68, 824

Glucose-6-phosphate Dehydrogenase Activity and Hemoglobin Types

Dr. Boyer at Johns Hopkins Hospital reported that all subjects examined had normal glucose-6-phosphate dehydrogenase activity. On the starch gel electrophoresis all were of a uniform glucose-6-phosphate dehydrogenase electrophoretic type Class B. This is the type observed in all Americans of European ancestry and in 70% of Americans of mixed African and European ancestry.

Electrophoretic studies of hemoglobin showed that all Marshallese subjects examined had type AA_2.

Blood Volume Studies

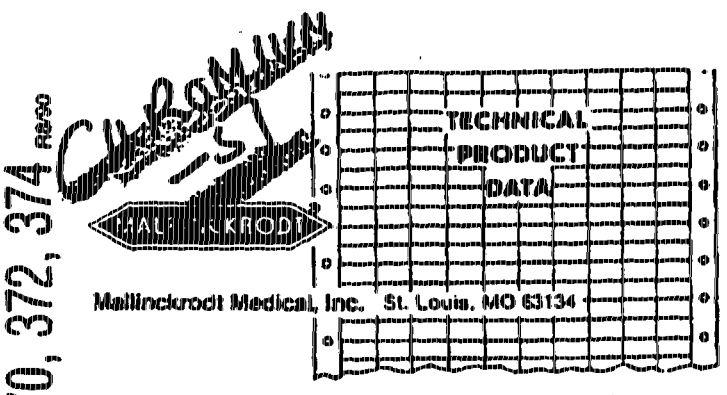
During the 1961 and 1962 surveys, blood volume determinations, with use of Cr^{51}-labeled sodium chromate, were performed on 25 normal Micronesian and Caucasian persons living in the Marshall Islands for 1 yr or longer. Table 15 shows the data for 23 of these on red cell mass and plasma volume based on body weight. From these data it appears that there was a significant reduction in red cell mass and/or plasma volume in 15 of 23 subjects, both Marshallese and Americans. During the anticipated 1963 survey, it is planned to repeat these studies in conjunction with estimations of lean body mass by use of tritiated water. Evaluation of the above results will be withheld until completion of the 1963 survey.

Immunoelectrophoretic Studies

Immunoelectrophoretic analyses were carried out on a number of Marshallese sera. These results are shown in Table 16. Dr. R. Bütler, who carried out these analyses, reported that "in summary we have found neither a paraproteinemia nor a typical picture of antibody-deficiency-syndrome. The high frequency of increases of some of the immunoglobulins is perhaps a typical sign of the investigated population."

Enclosure 4

370, 372, 374 R/90



SODIUM CHROMATE Cr 51 INJECTION

Diagnostic — For Intravenous Use

DESCRIPTION

Sodium Chromate Cr 51 ($Na_2{}^{51}CrO_4$) Injection is available for diagnostic use as a sterile, non-pyrogenic solution. Each milliliter contains 3.7 megabecquerels (100 microcuries) chromium-51 on the calibration date, and 0.5 milligrams sodium bicarbonate as a buffer. The pH is adjusted to between 7.5 and 8.5 with hydrochloric acid or sodium hydroxide. The specific activity is at least 370 megabecquerels (10 millicuries) per milligram of sodium chromate.

Physical Characteristics

Chromium-51 decays by electron capture with a physical half-life of 27.7 days.[1] The principal photon useful for detection is listed in Table 1.

Table 1: Principal Radiation Emission Data[1]

Radiation	*Mean Percent Per Disintegration*	*Energy (keV)*
Gamma-1	9.83	320.1

External Radiation

The specific gamma ray constant for chromium-51 is 0.18 R/mCi-hr at 1 cm. The first half-value thickness is 0.17 cm of lead (Pb). A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of a 1.68 cm thickness of Pb will decrease the external radiation exposure by a factor of about 1,000.

[1]Kocher, David C., "Radioactive Decay Tables," DOE/TIC-11026, page 74 (1981).

Table 2: Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	*Coefficient of Attenuation*
0.17	0.5
0.56	10^{-1}
1.12	10^{-2}
1.68	10^{-3}
2.23	10^{-4}

To correct for radioactive decay of chromium-51, the fractions that remain at selected time intervals after the date of calibration are shown in Table 3.

Table 3. Physical Decay Chart; Chromium-51, Half-Life 27.7 Days

Days	*Fraction Remaining*	*Days*	*Fraction Remaining*	*Days*	*Fraction Remaining*
0*	1.000	11	0.759	22	0.577
1	0.975	12	0.741	23	0.562
2	0.951	13	0.722	24	0.549
3	0.928	14	0.704	25	0.535
4	0.905	15	0.687	26	0.522
5	0.882	16	0.670	27	0.509
6	0.861	17	0.654	28	0.496
7	0.839	18	0.637	29	0.484
8	0.819	19	0.622	30	0.472
9	0.798	20	0.606	60	0.223
10	0.779	21	0.591	90	0.105

*Calibration Time

CLINICAL PHARMACOLOGY

Chromium is present in the hexavalent (plus 6) state, in which form it readily penetrates the red blood cell, attaches to the hemoglobin, and is reduced to the trivalent (plus 3) state. This state is maintained until the red blood cell is sequestered by the spleen, at which time the chromium is released to the plasma and is readily excreted in the urine. In the trivalent state, chromium-51 is not re-utilized for tagging of additional red blood cells. Since the product has a high specific activity, adequate red blood cell tagging is secured in minimum time without demonstrable effect on cell life.

INDICATIONS AND USAGE

Sodium Chromate Cr 51 Injection may be used in the determination of red blood cell volume or mass, the study of red blood cell survival time, and evaluation of blood loss.

CONTRAINDICATIONS

None known.

WARNINGS

None known.

PRECAUTIONS

General

As in the use of any radioactive material, care should be taken to minimize radiation exposure to the patient, consistent with proper patient management, and to insure minimum radiation exposure to occupational workers.

In order to preclude or minimize the possibility of contamination and increased fragility of the tagged red blood cells, sterile technique must be employed throughout the collection, tagging, rinsing, suspending, and injection of the blood cells. Also, the number of washes and transfers should be kept to a minimum, and only sterile, pyrogen-free isotonic diluent should be employed throughout the tagging procedure.

Specific activity should be not less than 370 megabecquerels (10 millicuries) per milligram of sodium chromate at the time of use. Do not use after expiration date stated on label.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenesis, mutagenic potential, or whether this drug affects fertility in males or females.

nancy Category C

al reproductive studies have not been conducted with Sodium Chromate . It is also not known whether Sodium Chromate Cr 51 can cause *fetal* when administered to a pregnant woman or can affect *reproduction* ity. Sodium Chromate Cr 51 should be given to a pregnant woman only if y needed.

ly, examinations using radiopharmaceuticals, especially those elective in e, of a woman of childbearing capability should be performed during the ew (approximately 10) days following the onset of menses.

ing Mothers

e Chromium-51 is excreted in human milk during lactation, formula ngs should be substituted for breast feedings.

atric Use

ty and effectiveness in children have not been established.

EACTIONS

...reactions specifically attributable to the use of this drug have been rted.

SAGE AND ADMINISTRATION

usual dosages in the average adult patient (70 kg) are as follows:

The determination of red blood cell volume or mass: 0.37 to 1.11 megabecquerels (10 to 30 microcuries).

The determination of red blood cell survival time: 5.55 megabecquerels (150 microcuries).

The evaluation of blood loss: 7.4 megabecquerels (200 microcuries).

:nteral drug products should be inspected visually for particulate matter discoloration prior to administration. Do not use if contents are turbid.

patient dose should be measured by a suitable radioactivity calibration em immediately prior to administration.

liation Dosimetry

estimated absorbed radiation doses[1] to an average patient (70 kg) from an avenous injection of a maximum dose of 7.4 megabecquerels (200 micro-ies) of Sodium Chromate Cr 51 are shown in Table 4.

:thod of Calculation: "S" Absorbed Dose per Unit Cumulated Activity for lected Radionuclides and Organs, MIRD Pamphlet No. 11 (1975).

Table 4. Absorbed Radiation Dosage

Tissue	*Sodium Chromate Cr 51*	
	mGy/7.4 MBq	*rads/200 µCi*
Blood	2.0	0.30
Spleen	26.4	3.64
Testes	0.66	0.066
Ovaries	0.66	0.066
Total-body	0.55	0.055

HOW SUPPLIED

370 Sodium Chromate Cr 51 Injection is supplied at a concentration of approximately 3.7 megabecquerels (100 microcuries) per milliliter in vials containing approximately 9.25 megabecquerels (250 microcuries) as of the date of calibration. The specific activity is greater than 370 megabecquerels (10 millicuries) per milligram of sodium chromate within the expiration time of the product stated on the label.

372 A-C-D (Anticoagulant-Citrate-Dextrose) Solution (Modified) is supplied in 100-milliliter vials containing 10 milliliters of solution for tagging red blood cells with Sodium Chromate Cr 51. Each milliliter contains 8 milligrams of citric acid (anhydrous), 25 milligrams sodium citrate (dihydrate) and 12 milligrams dextrose (anhydrous). Ratio of ingredients differs from USP Formulas.

374 Red Cell Tagging Kit

Kit Contains:

1 vial – Sodium Chromate Cr 51 Injection containing approximately 9.25 megabecquerels (250 microcuries) as of the date of calibration.

1 vial – A-C-D Solution (Modified), 100-milliliter vial containing 10 milliliters of Anticoagulant-Citrate-Dextrose Solution (Modified).

1 ampoule – Ascorbic Acid Injection containing 1000 milligrams in 10 milliliters.

10 – Counting Vials

Storage and Handling

Store at room temperature (below 86°F/30°C).

Storage, handling and disposal of Chromium-51 solutions should be controlled in a manner that is in compliance with the appropriate regulations of the governmental agency authorized to license the use of this radionuclide.

DIRECTIONS FOR USE (TEST PROCEDURE)

NOTE 1: Wear waterproof gloves during the entire red cell tagging procedure and during subsequent patient dose withdrawals.

NOTE 2: Make transfers of Chromium-51 solutions during the tagging procedure and during subsequent injections of radiolabeled blood cells with adequately shielded syringes.

NOTE 3: Maintain adequate shielding of the radiolabeled blood cells by using a lead vial shield and cover.

Various procedures may be employed in performing the diagnostic tests for Sodium Chromate Cr 51 is indicated. The following outlines specific procedures which may be elected in performing these tests.

Red Cell Volume

The following procedure provides a direct measurement of the red blood cell component, and the whole blood volume is inferred from the venous hematocrit. The plasma chromium-51 radioactivity is excluded by calculation, thereby obviating the aseptic washing of the red blood cells.

Procedure:

1. With A-C-D solution from the A-C-D tagging vial, wet a 20-ml syringe and then use the syringe to withdraw 15 ml of blood from the antecubital vein.
2. Slowly and gently (to prevent hemolysis) aseptically inject the contents of the syringe into the vial of A-C-D solution.
3. With a 10-ml syringe aseptically add approximately 3.7 MBq (100 μCi) of Sodium Chromate Cr 51 Injection to the blood-A-C-D mixture.
4. Gently mix the blood by intermittent swirling every 5 to 10 minutes. Allow to tag at room temperature for 30 minutes.
5. With a 1-ml syringe aseptically add 30 to 50 mg of ascorbic acid injection to the vial, mix gently, and allow to stand for 5 minutes.
6. After gently mixing, withdraw **exactly** 10 ml of the tagged red blood cell (RBC) suspension, and inject intravenously into the patient.

7. Determine the hematocrit of the remaining Tagged RBC Suspension (A).
8. Pipet 1 ml of the tagged RBC suspension into a 100-ml volumetric flask and dilute to 100 ml with water. Mix thoroughly and pipet 4 ml into a counting vial. This is the Whole Blood Standard (B).
9. Centrifuge the remaining tagged RBC suspension, and pipet 1 ml of the plasma into a 100-ml volumetric flask, and dilute to 100 ml with water. Mix thoroughly, and pipet 4 ml into a counting vial. This is the Plasma Standard (C).
10. Ten to twenty minutes post injection withdraw approximately 20 ml of blood from the patient with a sterile, evacuated container containing an anticoagulant.
11. Pipet 4 ml of the whole blood into a counting vial. This is the Patient Whole Blood Sample (D).
12. Remove a sample for a Patient Hematocrit (E) and centrifuge the remaining blood.
13. Pipet 4 ml of plasma into a counting vial. This is the Patient Plasma Sample (F).
14. Count the: Whole Blood Standard (B)
    Plasma Standard (C)
    Patient Whole Blood Sample (D)
    Patient Plasma Sample (F)
    Background

Subtract background from B, C, D, F. Counting times should be equal and of sufficient length to provide a minimum of 10,000 counts.

Calculations:

A = Hematocrit of Tagged RBC Suspension (step 7)
B = Net Whole Blood Standard Count
C = Net Plasma Standard Count
D = Net Patient Whole Blood Sample Count
E = Patient Hematocrit (step 12)
F = Net Patient Plasma Sample Count

$$\text{Red Cell Volume (ml)} = \frac{[B - C(1 - A)]\,E}{D - F(1 - E)} \times 1000$$

$$\text{Whole Blood Volume (ml)} = \frac{\text{Red Cell Volume (ml)}}{\text{Patient Hematocrit}}$$

Plasma Volume (ml) = Whole Blood Volume (ml) – Red Cell Volume (ml)

Red Cell Survival

Procedure:

1. With A-C-D solution from the A-C-D tagging vial, wet a 20-ml syringe and then use the syringe to withdraw 15 ml of blood from the *antecubital* vein.
2. Slowly and gently (to prevent hemolysis) aseptically inject the contents of the syringe into the vial of A-C-D solution.
3. With a 10-ml syringe aseptically *add approximately* 7.4 MBq (200 μCi) of Sodium Chromate Cr 51 Injection to the blood-A-C-D mixture.
4. Gently mix the blood by intermittent swirling every 5 to 10 minutes. Allow to tag at room temperature for 30 *minutes*.

   Withdraw 20 ml of the tagged RBC suspension and inject intravenously into the patient.

6. At 24 hours post injection and every 2 to 3 days thereafter for a minimum of 30 days or until a half-time is reached, withdraw 10 ml of blood into a sterile, evacuated container containing an anticoagulant. Determine the hematocrit of each sample.

   NOTE: Each sample should be labeled with the date and time of withdrawal. Each withdrawal should be at approximately the same time each day. Frequency of sampling depends primarily on convenience. For statistical accuracy a minimum of 10 samples should be obtained.

7. Pipet 4 ml of each sample into a counting vial and label accordingly.
8. Count all samples at the same time to negate the effect of radioactive decay. Count and subtract background.

Calculations:

The calculations are based on using the 24-hour sample as 100% and making it the *starting point*. All other samples are calculated as a percent of the 24-hour sample, and indicate the percent remaining. If later samples have hematocrits different from the 24-hour sample, the correction below should be made.

$$\% \text{ Remaining} = \frac{\text{Net Whole Blood Count (each sample)}}{\text{New Whole Blood Count (at 24 Hours)}} \times \frac{\text{Hematocrit (at 24 hours)}}{\text{Hematocrit (each sample)}} \times 100$$

As indicated, the above calculation should be made on each sample individually. Upon completion of the calculation, the percent remaining should be plotted on the logarithmic scale against time on semi-logarithm paper. Draw a best-fit straight line through the points. The red cell survival time is determined from the graph by finding the time at which the straight line reached 50 percent.

Normal Range: Normal 28 to 40 days
Abnormal Less than 28 days

The U.S. Nuclear Regulatory Commission has approved distribution of this radiopharmaceutical to persons licensed to use byproduct material listed in Section 35.100, and to persons who hold an equivalent license issued by an Agreement State.

ENCLOSURE 5

The Medical Research Center

725173

Brookhaven National Laboratory

BROOKHAVEN NATIONAL LABORATORY

Upton, L. I., New York

MEMORANDUM

DATE: July 29, 1955

REPOSITORY Records Holding Area Bldg 494

COLLECTION Protocols - Clinical

BOX No. 4

FOLDER Human Protocols 1950-1963

TO: BNL Committee on Use of Radioactive Isotopes in Humans

FROM: J. A. James, M. D.

SUBJECT: Proj. H-39: Use of Cr^{51} as tracer in children.

It has been observed that the infusion of 25 percent salt-poor albumin into one nephrotic child caused a marked decrease in all plasma lipid fractions. Albumin causes a marked increase in plasma volume, and it is desirable to determine how much of the change in lipid concentration could be accounted for by dilution and how much may represent a more significant change in lipid metabolism.

It is proposed that the plasma volume be measured at the beginning and end of the course of albumin infusions (about 7 - 10 days) using Cr^{51} as $CrCl_3$.

Method

It has been calculated that 20 μc Cr^{51} would deliver a dose of 600 mr to the blood, assuming no excretion and no loss from the plasma compartment. Since such losses are considerable it is suggested that 50 μc could be given safely on two occasions within one month.

Reference:

Frank, H. and Gray, S.J. Measurement of plasma volume by radiochromic chloride, Jnl of Clin. Invest. 32, 991 (1953).

Approved:

Lee E. Farr, M.D.

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